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(54) **AMPHIPHILIC DRUG-OLIGOMER CONJUGATES WITH HYDROYZABLE LIPOPHILE COMPONENTS AND METHODS FOR MAKING AND USING THE SAME**

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(58) **Field of Search** 424/85.1, 85.2, 424/85.4, 85.5, 85.6, 85.7, 94.3, 178.1, 179.1, 193.1, 194.1; 435/188; 514/2, 3, 8, 12, 21, 476, 506, 579, 613, 715; 530/300, 303, 322, 345, 350, 351, 403, 405, 406, 409, 410, 411

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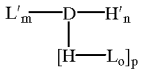
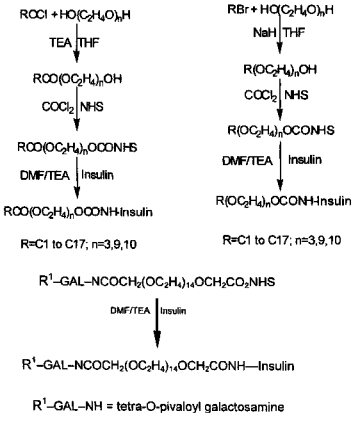
(57) **ABSTRACT**

The invention provides a drug-oligomer conjugate having the following general formula:



wherein D is a therapeutic drug moiety; H and H' are each a hydrophilic moiety, independently selected from the group consisting of straight or branched PEG polymers having from 2 to 130 PEG subunits, and sugars; L is a lipophilic moiety selected from the group consisting of alkyl groups having 2–26 carbon atoms, cholesterol, adamantane and fatty acids; o is a number from 1 to the maximum number of covalent bonding sites on H; m+n+p together have a value of at least one and not exceeding the total number of covalent bonding sites on D for the —H', —L and —H—L substituents; the H—L bond(s) are hydrolyzable and the D—L' bond(s), when present, are hydrolyzable; the conjugate being further characterized by one of the following: (i) m is 0 and p is at least 1; (ii) n is 0 and p is at least 1; (iii) m and n are each 0 and p is at least 1; (iv) p is 0 and m and n are each at least 1. The therapeutic drug moiety is preferably a therapeutic protein or peptide, preferably insulin or a functional equivalent thereof.

60 Claims, 3 Drawing Sheets



Synthesis Scheme for Drug–Oligomer Conjugates